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Appendix F Chemicals

This appendix presents basic information about chemical risk assessment for carcinogens and noncarcinogens. The information is intended to serve as a basis for understanding the toxicity associated with possible releases from the Oak Ridge Reservation (ORR) and is not a comprehensive discussion of chemicals and their effects on human health and the environment.

F.1. Perspective on Chemicals

The lives of modern humans have been greatly improved by the development of chemicals such as pharmaceuticals, building materials, housewares, pesticides, and industrial chemicals. Through the use of chemicals, we can increase food production, cure diseases, build more efficient houses, and send people into space. At the same time, we must be cautious to ensure uncontrolled and over-expanded use of chemicals does not endanger our own existence (Diamanti-Kandarakis et al. 2009, Duruibe et al. 2007, Li et al. 2018, Sunderland et al. 2019).

Just as all humans are exposed to radiation in their normal daily routines, humans are also exposed to chemicals. Some potentially hazardous chemicals exist in the natural environment. In many areas of the country, soils contain naturally elevated concentrations of metals such as selenium, arsenic, or molybdenum, which may be hazardous to humans or animals. Even some of the foods we eat contain natural toxins. Aflatoxins are found in chili peppers, corn, millet, peanuts, rice, sorghum, sunflower seeds, tree nuts, and wheat. Cyanide is found in apple seeds. However, exposure to many more hazardous chemicals results from direct or indirect human actions. Building materials used in home construction may contain chemicals such as formaldehyde (in some insulation materials), asbestos (formerly used in insulation and ceiling tiles), and lead (formerly used in paints and gasoline). Some chemicals are present as a result of applying pesticides and fertilizers to soil. Other chemicals may have been transported long distances through the atmosphere from industrial sources and then deposited on soil or water.

F.2. Pathways of Chemicals from the Oak Ridge Reservation to the Public

Pathways are the routes or ways through which a person can encounter a chemical substance. Chemicals may be released to the air, soil, or water. Chemicals may also be released as liquid wastes, called effluents, which can enter streams and rivers.

People are exposed to chemicals by inhalation (breathing air), ingestion (intake of food, soil, or water), or dermal contact (touching soil or swimming in water). For example, fish that live in a river containing effluents may take in some of the chemicals present in the water. People eating fish and drinking water from the river would then be exposed to the chemicals. The public is not normally exposed to chemicals on ORR because access to the reservation is limited. However, chemicals released as a result of ORR operations can move through the environment to off-site locations, resulting in potential exposure of the public.

F.3. Toxicity

Toxicity refers to an adverse effect of a chemical on human health. Health effects from chemical exposures vary based on the chemical's toxicity. The toxic effect can be acute (a short-term, possible severe health effect) or chronic (a longer-term, persistent health effect). Although we ingest chemicals in food, water, and medications every day, toxic chemicals are typically nontoxic or harmless below certain concentrations or thresholds.

Chemical health effects due to toxicity are divided into two broad categories: adverse or systemic effects from noncarcinogens and cancer from carcinogens. The potential health hazards of noncarcinogens range from mild (e.g., skin irritation) to severe (e.g., death). Carcinogens cause or increase the incidence of malignant neoplasms or cancers. A chemical can have both carcinogenic and noncarcinogenic effects. Toxic effects can result from short-term or long-term chemical exposures.

Concentration limits or advisories are set by government agencies for some chemicals that are known or suspected to have adverse effects on human health. These concentration limits are used to calculate chemical doses that would not be harmful to individuals who are particularly sensitive to a chemical. These chemical doses are converted to slope factors to address carcinogenic risk and to reference doses to address noncarcinogenic hazards (Hayes and Kobets 2023)

F.3.1. Dose Terms for Carcinogens

A slope factor is a plausible upper-bound estimate of the probability of a response per daily dose of a chemical during a lifetime of exposure (70 years). The slope factor conservatively estimates the probability of cancer due to chemical exposure for an individual's lifetime to a particular concentration. Units are expressed as risk per dose in mg/kg-day.

A slope factor converts the estimated daily dose, averaged over a lifetime exposure, to the incremental risk of an individual developing cancer. Because it is unknown for most chemicals whether a threshold (an intake below which no adverse effect occurs) exists for carcinogens, units for carcinogens are set in terms of risk factors. The standard cancer benchmarks used by the US Environmental Protection Agency (EPA) range from 1 in 1,000,000 to 1 in 10,000 (i.e., 10^{-6} to 10^{-4}), depending on the subpopulation exposed. In other words, a certain chemical concentration in food or water could cause a risk of one additional cancer for every 1,000,000 (10^{-6} risk level) to 10,000 (10^{-4} risk level) exposed persons.

F.3.2. Dose Term for Noncarcinogens

A reference dose is an estimate of a daily chemical exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a period of exposure. Units are expressed as milligrams of chemical per kilogram of body weight per day (mg/kg-day). Reference dose values are derived from chemical intakes that resulted in no adverse effect or the lowest dose that showed an adverse effect in humans or laboratory animals.

Uncertainty factors are typically used in deriving reference doses. Uncertainty adjustments may be made to account for (1) interspecies variability in response when extrapolating from animal studies to humans; (2) response variability in humans; (3) uncertainty in estimating a no-effect level from a dose where effects were observed; (4) extrapolation from shorter duration studies to a full life-time exposure; and (5) data deficiencies (Dankovic et al., 2015). The use of uncertainty factors in deriving reference doses is thought to help protect sensitive human subpopulations.

F.3.3. Toxicity Value Sources

The slope factors and reference doses used for ORR calculations are selected from a tiered hierarchy system devised by EPA (EPA 2003). Values in the Integrated Risk Information System database, a Tier 1 toxicity value source, are considered to be validated and have undergone rigorous peer review and an EPA consensus review process. The EPA's Provisional Peer-Reviewed Toxicity Value database is a Tier 2 toxicity value source with values primarily derived for use in EPA's Superfund Program. Provisional Peer-Reviewed Toxicity Values are derived from a review of the relevant scientific literature using EPA methods, sources of data and guidance for value derivation. Tier 2 values have undergone rigorous peer review, but an EPA consensus review has not been performed. Tier 3 toxicity value sources include other sources of information and are used when Tier 1 or 2 values are not available for a contaminant. Multiple Tier 3 toxicity value sources are used on ORR including the Agency for Toxic Substances and Disease Registry Minimal Risk Levels, the EPA's Office of Pesticide Programs Human Health Benchmarks for Pesticides, EPA's Health Effects Summary Table, and other federal and state sources.

F.4. Measuring Chemicals

Environmental samples are collected in areas surrounding ORR and are analyzed for those chemical constituents most likely to be released from ORR. Chemical concentrations in liquids are typically expressed in milligrams or micrograms of chemical per liter of water (mg/L or µg/L, respectively); concentrations in solids, such as soil and fish tissue, are expressed in milligrams or micrograms of chemical per kilogram of sample material (e.g., mg/kg or µg/kg for soil or fish tissue).

The instruments used to measure chemical concentrations are sensitive; however, there are limits below which they cannot detect chemicals of interest. Concentrations below the reported analytical detection limits of the instruments are recorded by the laboratory as estimated values, which have a greater uncertainty than concentrations detected above the detection limits of the instruments. Concentrations that use these estimated values are indicated by the less-than symbol (<), which specifies that the value for a parameter could not be quantified at the analytical detection limit.

F.5. Risk Assessment Methodology

The methods for assessing the cancer risk and noncancer hazard resulting from exposure to a particular chemical are discussed in the following paragraphs.

Exposure Assessment

To estimate an individual's potential exposure via a specific exposure pathway, the daily dose of the chemical must be determined. For example, chemical dose (in units of mg of contaminant per kilogram of body weight per day) from drinking water and eating fish from the Clinch River is assessed in the following manner:

Clinch River surface water and fish tissue samples are analyzed to measure chemical contaminant concentrations. Estimated daily doses to the public are calculated by multiplying chemical concentrations measured in the samples by the surface water intake rate (liters/day) and fish ingestion rate (kg/day), respectively. The average daily intakes are then multiplied by the exposure duration (in years) and exposure frequency (days/year) and divided by an averaging time (365 days/year multiplied by a lifetime [70 years] for carcinogens or the exposure duration for noncarcinogens). The default exposure assumptions are conservative and, in many cases, may result in higher estimated daily doses than an individual would actually receive.

Calculation Method

Carcinogenic risk calculations use slope factors and daily doses averaged over a lifetime (70 years). To estimate the potential carcinogenic risk from ingestion of water and fish, the estimated average daily dose (mg/kg-day) is multiplied by the slope factor (risk per mg/kg-day), resulting in units of risk. As mentioned earlier, acceptable risk levels for carcinogens range from 10^{-6} (risk of developing cancer over a human lifetime is 1 in 1,000,000) to 10^{-4} (risk of developing cancer over a human lifetime is 1 in 10,000). Carcinogenic risks greater than 10^{-4} indicate a concern for adverse health effects or the need for further study.

Noncarcinogenic hazard calculations use reference doses and daily doses averaged over the exposure duration. To calculate the potential hazard from ingestion of water and fish, the estimated average daily dose (mg/kg-day) is divided by the RfD (mg/kg-day), resulting in a unitless value called a hazard quotient. Hazard quotient values less than 1 indicate an unlikely potential for adverse noncarcinogenic health effects; hazard quotient values greater than 1 indicate a concern for adverse health effects or the need for further study.

F.6. References

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